Amendments to the Claims:

This listing of claims replaces all prior versions and listings of claims in the application:

Listing of Claims:

1. – 10. (cancelled)

11. (previously presented) A method of evaluating the deacetylation of a substrate in the presence of a Sir2 protein, NAD or an NAD-like compound and an agent, the method comprising:

a) combining a substrate that comprises an acetylated amino acid side chain, an isolated or recombinantly produced Sir2 protein, NAD or an NAD-like compound and an agent to be tested, thereby producing a combination; and

b) determining if the acetylated amino acid side chain in the substrate is deacetylated.

12. – 168. (canceled)

169. (currently amended) The method of claim 11 wherein ~~the determining~~ step (b) comprises electron-spray mass spectroscopy.

170. (previously presented) The method of claim 11 further comprising comparing deacetylation of the substrate in the presence of the agent to deacetylation of the substrate in the absence of the agent, wherein a difference in substrate deacetylation indicates that the agent alters Sir2 protein deacetylase activity.

171. (previously presented) The method of claim 11 wherein the Sir2 protein is a human Sir2 protein.

172. (previously presented) The method of claim 11 wherein the Sir2 protein is a murine Sir2 protein.

173. (previously presented) The method of claim 11 wherein the Sir2 protein is a fusion protein.

174. (previously presented) The method of claim 11 wherein the substrate is a fragment of a histone that comprises the N-terminal tail of a histone protein.

175. (previously presented) The method of claim 174 wherein the histone protein is histone H3.

176. (currently amended) The method of claim 175 wherein ~~the fragment is acetylated at positions corresponding to the lysine amino acid residue is~~ the N-terminal tail of histone H3 is acetylated at lysine 9 and/or lysine 14 ~~of H3 histone~~.

177. (previously presented) The method of claim 11 wherein the substrate is a histone protein.

178. (previously presented) The method of claim 177 wherein the histone protein is selected from the group consisting of an H2B, H3 and H4 histone protein.

179. (previously presented) The method of claim 177 wherein the histone protein is acetylated on a lysine amino acid residue.

180. (previously presented) The method of claim 179 wherein the histone protein is histone H4 and the protein is acetylated on lysine 16 of histone H4.

181. (currently amended) The method of claim 11 wherein the acetylated amino acid ~~side~~ is an acetylated lysine amino acid.

182. (previously presented) The method of claim 11 wherein the Sir2 protein is an isolated Sir2 protein.

183. (previously presented) The method of claim 11 wherein the Sir2 protein is a recombinantly produced Sir2 protein.

184. (previously presented) The method of claim 11 wherein the combination comprises $MgCl_2$.

185. (currently amended) The method of claim 11 wherein the combination comprises dithiothreitol (DTT).

186. (previously presented) The method of claim 11 further comprising formulating the agent with a pharmaceutically acceptable carrier to provide a pharmaceutical composition.

187. (previously presented) The method of claim 186 wherein the pharmaceutically acceptable carrier comprises a carbohydrate.

188. (previously presented) The method of claim 11 wherein the combination comprises NAD.

189. (previously presented) The method of claim 11 wherein the Sir2 protein is a Sir2α protein.

190. (previously presented) The method of claim 189 wherein the Sir2α protein comprises SEQ ID NO:12.

191. (previously presented) A method of evaluating the deacetylation of a substrate in the presence of a human Sir2 protein, NAD, and an agent, the method comprising:

a) providing a mixture comprising a substrate that comprises an acetylated amino acid side chain, an isolated or recombinantly produced human Sir2 protein, NAD, and an agent to be tested; and

b) determining if the acetylated amino acid side chain in the substrate is deacetylated.

192. (previously presented) The method of claim 191 wherein the mixture comprises $MgCl_2$.

193. (currently amended) The method of claim 191 wherein the mixture comprises dithiothreitol (DTT).

194. (previously presented) The method of claim 11 or 191 wherein the SIR2 protein is produced in *E. coli.*

195. (previously presented) The method of claim 11 or 191 wherein the agent is a protein.

196. (previously presented) The method of claim 11 or 191 wherein the agent is a peptide.

197. (previously presented) The method of claim 11 or 191 wherein the agent is naturally occurring.

198. (previously presented) The method of claim 11 or 191 wherein the agent is non-naturally occurring.

199. (previously presented) The method of claim 11 or 191 wherein the agent is chemically synthesized.

200. (previously presented) The method of claim 11 or 191 wherein the agent is a carbohydrate.

201. (previously presented) The method of claim 11 or 191 wherein the agent is a steroid.

202. (previously presented) The method of claim 11 or 191 wherein the agent is a lipid.

203. (previously presented) The method of claim 11 or 191 wherein the agent is an anion.

204. (previously presented) The method of claim 11 or 191 wherein the agent is a cation.

205. (previously presented) The method of claim 11 or 191 wherein the agent is an oligonucleotide.

206. (previously presented) The method of claim 195 wherein the agent is an antibody.

207. (previously presented) The method of claim 191 wherein the Sir2 protein is an isolated Sir2 protein.

208. (previously presented) The method of claim 191 wherein the Sir2 protein is a recombinantly produced Sir2 protein.

209. (currently amended) A method of evaluating deacetylation of a substrate in the presence of a Sir2 core domain, and NAD, the method comprising:

a) providing a mixture comprising a substrate that comprises an acetylated lysine amino acid side chain, a recombinantly produced protein that comprises a human SIR2 core domain, and NAD; and

b) determining if the acetylated amino acid side chain in the substrate is deacetylated.

210. (cancelled)

211. (previously presented) The method of claim 209 wherein the mixture comprises $MgCl_2$.

212. (currently amended) The method of claim 209 wherein the mixture comprises dithiothreitol (DTT).

213. (previously presented) The method of claim 209 wherein the recombinantly produced protein is a fusion protein.

214. (previously presented) The method of claim 209 wherein the recombinantly produced protein is produced in *E. coli*.

215. (new) A method of evaluating deacetylation of a substrate in the presence of a Sir2 core domain, and NAD, the method comprising:

a) providing a mixture comprising a substrate that comprises an acetylated lysine amino acid side chain, a recombinantly produced protein that comprises a SIR2 core domain comprising SEQ ID NO:4, and NAD; and

b) determining if the acetylated amino acid side chain in the substrate is deacetylated..

216. (new) A method of evaluating deacetylation of a substrate in the presence of a Sir2 core domain, and NAD, the method comprising:

a) providing a mixture comprising a substrate that comprises an acetylated lysine amino acid side chain, a recombinantly produced protein that comprises a fragment of a SIR2 protein, and NAD, wherein the fragment of the SIR2 protein comprises GAG(V/I)S(T/V)S (L/C/A)GIPDFRS (SEQ ID NO:38) and YTQNID (SEQ ID NO: 28) and NAD-dependent deacetylase activity; and

b) determining if the acetylated amino acid side chain in the substrate is deacetylated.

217. (new) The method of claim 209 wherein the fragment is a fragment of a human SIR protein.

218. (new) The method of claim 209 wherein the mixture further comprises an agent to be tested.

219. (new) The method of claim 216 wherein the mixture further comprises an agent to be tested.